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Schizophrenia and HLA: a review

Padraig Wright^a, Vishwajit L. Nimgaonkar^b, Peter T. Donaldson^c and Robin M. Murray^a^a Department of Psychological Medicine, Institute of Psychiatry and King's College Hospital, De Crespigny Park, London SE5 8AF, UK^b Western Psychiatric Institute and Clinic, University of Pittsburgh, 3811 O'Hara Street, Pittsburgh, PA 15213, USA^c Centre for Liver Research, The School of Clinical Medical Sciences, University of Newcastle, Framlington Place, Newcastle-upon-Tyne NE2 4HH, UK


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Abstract

A number of reports of genetic association of human leucocyte antigens (HLA) and alleles with schizophrenia have recently been published. A schizophrenia locus on chromosome 6p near the HLA region has also been reported, on the basis of linkage studies. We have therefore reviewed the investigations of association of HLA with schizophrenia published from 1974 to date, and have also briefly reviewed the chromosome 6p linkage studies. Two or more groups of investigators have reported association of each of the following HLA antigens or alleles with schizophrenia — A9 or its A24

subspecificity, A28, A10, DRB1*01 and DRw6. However, these results may represent Type I errors caused by small sample size, inappropriate diagnostic, laboratory and/or statistical methodology, and/or incorrectly chosen comparison subjects. Hypothesis-driven negative associations of DRB1*04 and DQB1*0602 with schizophrenia have also been reported. Taken together, however, HLA association investigations provide only weak evidence for the existence of either resistance or susceptibility loci for schizophrenia close to the HLA region at the 6p21.3 band and, indeed, recently reported investigations that controlled for most of these confounders found no evidence of association. Linkage studies suggest that a susceptibility locus may exist and that it may be within the HLA region, but again the evidence is far from conclusive. Further HLA association investigations should employ operational diagnostic criteria, comparison subjects screened for illness and HLA genotyping, and should include both association studies of candidate alleles and transmission disequilibrium and haplotype relative risk studies.

Author Keywords: Autoimmunity; Genetic association; HLA; Review; Schizophrenia; Schizophrenia locus

 Corresponding author. Tel.: +44-171-9193129; fax: +44-171-7019044

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